Federal Regulations and Good Clinical Practice (GCP)

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Objectives

☐ Compare and contrast regulations and ethical principles of human research
☐ Review US regulatory backdrop and ethical underpinnings
☐ Clarify WMA’s Declaration of Helsinki
☐ Discuss ICH and Good Clinical Practice
Ethical Foundations of Human Subjects Research

- Nuremberg Code (1949)
- Belmont Report (1979)
- Declaration of Helsinki (1964, updated 2000)
Belmont Report Ethical Principles

- Respect for Persons
- Beneficence
- Justice

- Contains the ethical principles upon which the U.S. Federal regulations for protection of human subjects are based
National Research Act

- Enacted in 1974
- Established National Commission for Protection of Human Subjects of Biomedical and Behavioral Research
  - Belmont Report
- Established the IRB system for regulating research
U. S. Regulations

- 45CFR46
- Title 45: Public Welfare
- Part 46: Protection of Human Subjects
- Basic HHS Policy for Protection of Human Research subjects
- Aka “The Common Rule”
U.S. Regulations

- 21 CFR: FDA
- 21CFR50: Protection of Human Subjects, Informed Consent
- 21CFR56: IRBs (organization, membership, functions and operations, records and reports, non-compliance)
U.S. Regulations

- 21CFR 312: Investigational Drugs
- Form 1571: IND application
- Form 1572: Investigator qualifications and responsibilities assumed
- Aka “the hanging paper” (Dunn and Chadwick 2002)
Worldwide Guidance

- Declaration of Helsinki (1964…2000)
- Ethical Principles for Medical Research Involving Human Subjects
- World Medical Association code
- Directed at physicians doing medical research
- Primary purpose of medical research is to improve prophylactic, diagnostic, and therapeutic procedures and the understanding of the etiology and pathogenesis of disease
Declaration of Helsinki

☐ Emphasis on physician as caregiver
☐ Emphasis on careful assessment of risks and benefits
☐ Informed consent and ERCs
☐ Controversial standard of best possible therapy limits use of placebo
The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is a unique project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration.
ICH

- The purpose is to make recommendations on ways to achieve greater harmonization in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines.
E6: Good Clinical Practice: Consolidated Guidance

- An international ethical and scientific quality standard for designing, conducting, monitoring, recording, auditing, analyzing, and reporting drug trials that involve participation of human subjects
Good Clinical Practice

- Compliance with this standard provides public assurances that the rights, safety and well-being of trial subjects are protected, consistent with the Declaration of Helsinki, and that the clinical trial data are credible.

- Provide a unified standard to facilitate internal acceptance of clinical data by the regulatory authorities in these jurisdictions.
How are the principles applied?

- Careful review of the protocol
  - Review of study design and methodology
  - Inclusion/Exclusion Criteria
  - DSMP and Stopping Rules
  - Risks/Benefits
  - Consent Process
  - In Case of Injury Section
How are the principles applied?

- Careful review of the consent form
  - Purpose
  - Research Procedures
  - Risks
  - Anticipated Benefits
  - Alternative Treatments
  - Voluntariness
Conclusion

- Understanding basic ethical principles guides adherence to regulations
- International endorsement of essentially universal principles as stated in Belmont and Helsinki